REMARKS

Claims 1, 3, 4 and 6 are currently pending in this application. Claims 2, 5 and 7 were previously canceled without prejudice or disclaimer. Claim 1 has been amended.

Applicants thank the Examiner Sasan and her supervisor Sheikh for conducting an in-person interview with Applicants' undersigned representative on April 5, 2010. As discussed, Applicants present herein details of the unexpectedly superior results acquired by the presently claimed patch formulation with regard to the skin permeation rate and adhesion, cohesion and/or stability properties, as supported by the originally filed specification. Further, as suggested by the Examiners, Applicants have amended claim 1 to recite the improved properties achieved by the present claims, namely the limitation, "wherein the patch is configured to have a skin permeation rate of from about 1.5 $\mu g/cm^2/hr$ to about 3.2 $\mu g/cm^2/hr$ and to have improved adhesion, cohesion or stability." Claim 1 has further amended to replace the term "nitrogen-including" to read "nitrogen-containing," as discussed in the interview. Support for the amendments can be found throughout the specification, particularly Examples 4 and 5.

The amendments are for the sole reason of advancing prosecution. Applicants, by amending the claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert the original scope of the claims amended herein in a continuing application.

No new matter has been introduced to this application within the meaning of 35 U.S.C. §132.

In view of the following, further and favorable consideration is respectfully

requested.

I. Claims Rejections - 35 U.S.C. § 103(a)

The Examiner rejects claims 1, 3, 4 and 6 under 35 U.S.C. §103(a) as being unpatentable over Miranda et al. (U.S. Patent No. 5,656,286), in view of Hoffman (US Patent No. 5,820,876). As the basis for this rejection, the Examiner asserts in relevant part of the Official Action:

> Miranda does not expressly teach 2-ethylhexyl acrylate-vinyl acetate copolymer. Hoffmann teaches a transdermal therapeutic system for supplying active substances to the skin. The active substances reservoir matrix can be a rubber material such as styrene-isoprene-styrene (SIS) block copolymer. Adhesive materials including a self-crosslinking acrylate copolymer, e.g., of 2-ethylhexyl acrylate-vinyl acetate and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from ROHM) are disclosed (col. 7, lines 1-8). It would have been obvious to one of ordinary skill in the art at the time the inventions was made to make a transdermal drug delivery composition with SIS block copolymers as rubber-based pressure-sensitive adhesives and butyl methacrylate that is copolymerizable with methacrylic acid and dimethylaminoethyl methacrylate as suggested by Miranda, combine it with the transdermal composition with SIS block copolymer, copolymer of 2-ethylhexyl acrylate and vinyl acetate, and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate as suggested by Hoffman, and produce the instant invention.
>
> … This (Applicant's argument) is not persuasive because the combination of Miranda and Hoffmann renders limitations of the patch formulation obvious and therefore, the results presented by Applicant are not unexpected. One of ordinary skill in the art would have found the adhesive nature of the combination of Miranda and Hoffmann obvious and expected since both references teach polymers for the same purpose, i.e., adhesion and cohesion.

Applicants respectfully traverse this rejection. To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme

Court recently held in *KSR International Co. v. Teleflex Inc., 550 U.S. 398 (2007)*, "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ... it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc.* v. *Chugai Pharm. Co.*, 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Further, a *prima facie* case of obviousness, if established, can be rebutted when the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *Dillion*, 919 F.2d at 692-93, 16 USPQ2d at 1901. When considering whether proffered evidence is commensurate in scope with the claimed invention, office personnel should not require the applicants to show unexpected results over the entire range of properties possessed by a chemical compound or composition. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to

rebut a *prima facie* case of obviousness. *Id.*

In the present application, however, a *prima facie* case of obviousness has note been established by the cited references against the presently pending claims since both the references together fail to teach or suggest all the limitations of the present claims, and any potential *prima facie* case of obviousness if established, is rebutted by the unexpected result of the present claims which is supported by the comparative data presented in the present specification.

Presently Pending Claims 1, 3, 4 and 6

Presently pending independent claim 1 as amended is directed to:

A patch, comprising:
a backing layer; and
an adhesive layer disposed on the backing layer, the adhesive layer comprising a drug and an adhesive base agent comprising
a styrene-isoprene-styrene block copolymer,
2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the weight ratio of the content of the styrene-isoprene-styrene block copolymer to 2-ethylhexyl acrylate-vinyl acetate copolymer is from ***1:1 to 9:1***,
a basic nitrogen-containing polymer comprising a basic nitrogen and having no adhesion properties at normal temperature, the basic nitrogen-containing polymer being selected from the group consisting of methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer, and polyvinyl acetal diethylamino acetate, and
an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid,
wherein ***the patch is configured to have a maximum skin permeation rate of from about 1.5 μg/cm^2/hr to about 3.2 μg/cm^2/hr*** and to have improved adhesion, cohesion or stability.

As demonstrated by the data in Tables 1-4 on pages 34-37 of the present specification, the claimed patch formulation has ***unexpectedly superior effects*** in the

skin permeation rate, and in adhesion, cohesion and stability properties, as compared to patch formulations lacking one or more of the copolymers recited in the presently pending claims.

Dependent claims 3, 4 and 6 each incorporate the features recited in claim 1 above, and further recite the features of: the solubility of the drug in water as being 1% or less; the drug, pergolide; and the use of an alicyclic saturated hydrocarbon-based tackifier in the adhesive layer, respectively.

Teachings of Miranda et al. and Hoffman – Both in combination fail to disclose all the elements of the present claims.

Miranda et al. describe a blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug to form a pressure-sensitive adhesive composition for a transdermal drug delivery system. As the Examiner indicates in the Official Action, Miranda et al. further describe a rubber-based pressure-sensitive adhesives containing styrene-isoprene-styrene (SIS) block copolymer (col. 11, lines 20-23); Miranda et al. describe that by varying the amount of each type of monomer added, the cohesive properties of the resulting acrylate polymer can be changed as is known in the art. (col. 10, lines 51-54).

However, ***nowhere*** do Miranda et al. disclose, teach or suggest "2-ethylhexyl acrylate-vinyl acetate (2-EHA-VA) copolymer," or the combined use of 2-EHA-VA copolymer with SIS block copolymer, and in the ratio of 1:1 to 9:1. Miranda et al. only describe each monomer of methyl methacrylate, butyl methacrylate and dimethylaminoethyl methacrylate. Miranda et al. do not describe a combination of 2-

EHA-VA copolymer and methyl methacrylate–butyl methacrylate–dimethylaminoethyl methacrylate (MM-BM-DAEM) terpolymer. In addition, Miranda et al. do not describe using 2-EHA-VA acetate copolymer and a basic nitrogen-including polymer together. Furthermore, Miranda et al. do not describe the skin permeation rate of from about 1.5 µg/cm2/hr to about 3.2 µg/cm2/hr for the patch formulation.

Hoffmann describes a novel therapeutic system with active substance depot for the administration of the active substance (col. 2, lines 37 and 38). For a reservoir matrix that can be used in the therapeutic system disclosed therein, Hoffmann generally describe that the reservoir can be a pressure-sensitive adhesive that can be a rubber material such as SIS block copolymer (col. 4, lines 4-6). In Example 1, Hoffmann further describe a pressure-sensitive adhesive containing a self-crosslinking acrylate copolymer, e.g., of 2-ethylhexyl acrylate, vinyl acetate, acrylic acid and titanium chelate ester (DUROTAC 280-2416) and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100).

However, ***nowhere*** does Hoffmann describe an adhesive containing "a combination of SIS block copolymer and 2-EHA-VA copolymer," and thus also one in the amount ratio of "1:1 to 1:9." Hoffmann only describes a potential use of a rubber-based pressure-sensitive adhesive and describes a specific adhesive composition containing DUROTAC 280-2416 (copolymer of 2-ethylhexyl acrylate, vinyl acetate, acrylic acid and titanium chelate ester) and EUDRAGIT E 100 (an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate). Hoffmann, however, does not specifically describe an adhesive containing the combination of SIS block copolymer

and 2-EHA-VA copolymer, and the ratio of 1:1 to 9:1 between the two polymers. Further, Hoffmann describes patch formulations containing separate and distinct layers. In particular, the Hoffmann reference describes patch formulations which contain an active substance distribution device (i.e., a reservoir matrix layer) and a separate and distinct fixing device (such as, a porous pressure sensitive adhesive layer). The Hoffmann reference does not describe the combination of components in a single layer of the embodied patch formulations as required by presently pending claim 1. Furthermore, like Miranda et al., Hoffmann does not disclose, teach or suggest the "skin permeation rate of from about 1.5 µg/cm2/hr to about 3.2 µg/cm2/hr," as is required by the present claims.

Accordingly, Applicants assert that Miranda et al. and Hoffmann, taken alone or in combination, ***fail to disclose all of the elements of the presently pending claims***, as required by *In re Wilson*. That is, neither the Miranda et al. nor the Hoffmann references either taken alone or in combination describe the weight ratio of the content of the SIS block copolymer to the content of the 2-EHA-VA copolymer, respectively; and wherein the weight ratio of the content of the SIS block copolymer to the 2-EHA-VA copolymer is from 1:1 to 9:1. Further, neither of the references describe the skin permeation rate of from about 1.5 µg/cm2/hr to about 3.2 µg/cm2/hr, as is required by the present claims.

Applicants further assert that there is no suggestion in the art to modify the combination of references to achieve the patch formulation of the presently pending claims with the specific components in their recited ratio. In view of the unexpected

superior effects of the presently claimed patch formulation as set forth below in detail, which are from the combination of all of three polymer components in a single adhesive layer and from the specific combination ratio of 1:1 to 1:9 between SIS block copolymer and 2-EHA-VA copolymer, Applicants also assert that there is no expectation of success to arrive at the present claims. Accordingly, a *prima facie* case of obviousness has not been established in the present application.

A showing of unexpected results is the hallmark of nonobviousness and has generally been held to be sufficient to overcome/rebut a prima facie case of obviousness.

Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *Dillion*, 919 F.2d at 692-93, 16 USPQ2d at 1901. "The principle applies most often to the less predictable fields, such as chemistry, where minor changes in a product or process may yield substantially different results." *In re Mayne*, 104 F.3d 1339, 1343 (Fed. Cir. 1997), quoting *In re Soni*, 54 F.3d 746, 750, 34 U.S.P.Q.2d 1684, 1687 (Fed. Cir. 1995). When considering whether proffered evidence is commensurate in scope with the claimed invention, office personnel should not require the applicants to show unexpected results over the entire range of properties possessed by a chemical compound or composition. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. *Id.*

In this regard, Applicants bring the Examiner's attention to the unexpectedly superior properties of the presently claimed patch formulation outlined in Tables 1-4 on pages 34-37 of the original specification which demonstrates the unexpectedly superior results of the present claims as compared to patch formulations lacking one or more of the copolymers recited in the present claims.

Specifically, Applicants point to the comparative data in the specification at page 35, line 5, to page 37, Table 3. The examples in Table 3 comprise combinations of: (A) a SIS block copolymer; (B) 2-EHA-VA copolymer; and (C) MM-BM-DAEM terpolymer. The present claims recite all three components: (A), (B), and (C).

The Examiner cites Miranda et al. as teaching components (A) + (C), the use of "SIS block copolymers, butyl methacrylate copolymerizable with methacrylic acid and dimethylaminoethyl methacrylate," but "does not expressly teach 2-ethylhexyl acrylate-vinyl acetate copolymer (B)." Thus, ***Miranda et al***., as used by the Examiner, can be reasonably considered as corresponding to ***Comparative Examples 12 and 15*** in Table 3, which include components ***(A) + (C), but not (B).***

The Examiner then cites the example in Hoffmann at col. 7, lines 1-8, as teaching components (B) + (C), an embodiment having "adhesive materials including a self-crosslinking acrylate copolymer, e.g. of 2-ethyl-hexyl acrylate, vinyl acetate and an acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from ROHM)." This particular embodiment does not expressly combine these adhesive components with component (A), a SIS block copolymer. Thus, ***Hoffman's*** example, as used by the Examiner, can be reasonably considered as corresponding to

Comparative Examples 13 and 16 in Table 3, which include components ***(B) + (C), but not (A).***

Maximum skin permeation rates for Examples 12 and 15 (corresponding to ***Miranda***) are ***0.7 and 0.8*** (μg/cm^2/hr), respectively. Maximum skin permeation rates for Examples 13 and 16 (corresponding to ***Hoffman***) are ***0.5 and 0.3*** (μg/cm^2/hr), respectively. In addition: adhesion, cohesion, and/or stability characteristics were found to be "bad' ("C") for all Examples 12, 13, 15, and 16.

Unexpectedly, maximum skin permeation rates for Examples 4 and 5 (corresponding to ***present claims reciting features (A), (B), and (C)***) are ***1.5 and 3.2*** (μg/cm^2/hr), respectively. Similarly unexpected: adhesion, cohesion, and/or stability characteristics were found to be "very good' ("A") for Examples 4 and 5.

Unexpectedly, examples 4 and 5, relevant to the claimed subject matter (components A + B + C), provide a ***permeation rate that is 3 and 10 times higher*** than the individual examples corresponding to the examples cited by the Examiner in Miranda (components A + C) and Hoffmann (components B + C), respectively. Moreover, this unexpected increase in permeation rate unexpectedly coincides with an improvement in adhesion, cohesion, and/or stability characteristics from "bad" to "very good."

Accordingly, the skilled artisan could ***not*** have predicted that the combination of Miranda with Hoffman, having suggested permeation rates of (0.7 + 0.5) or (0.8 + 0.3), and bad adhesion, cohesion, and stability characteristics, would have resulted in a composition having a permeation rate of 1.5 or 3.2, respectively, and unexpectedly very

good adhesion, cohesion, and stability characteristics.

Furthermore, as demonstrated by the expert's declaration of Kazunosuke Aida which was attached to the response of December 19, 2008, the presently claimed patch formulation shows unexpectedly superior results in cohesion properties when the weight ratio (A:B) of the SIS block copolymer (A) to 2-EHA-VA copolymer (B) is from 1:1 to 9:1. Comparative Example A is directed to the same composition for Example 1-3, except that its A:B ratio is 4:6, which is outside the 1:1 to 9:1 range recited in the present claims. Examples 1-3 and comparative example 1 show the same measurements provided in the specification in Table 1, on page 34. Clearly, patch examples 1-3, having an A:B ratio of 1:1 to 9:1, have an unexpectedly superior Cohesion properties as compared to Comparative Example A having an A:B ratio of only 4:6, which is outside the 1:1 to 9:1 range recited in the present claims.

Accordingly, nothing in any of the applied references, taken alone or in combination, renders claim 1, 3, 4 and 6 obvious within the meaning of 35 U.S.C. §103. Thus, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection.

II. Obviousness-Type Double Patenting Rejection

The final Official Action states that claims 1, 4 and 6 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-11 of copending U.S. Patent Application Serial No.

10/526,065.

The Examiner asserts that although the conflicting claims are not identical, they are not patentably distinct from each other. The Examiner notes that the instant claims are directed to a patch comprising a backing layer and an adhesive layer that is compounded with a drug and an adhesive base agent. The Examiner asserts that the claims of the copending U.S. Patent Application No. 10/526,065 also describe a patch comprising a backing layer and an adhesive layer compounded with an adhesive agent and pergolide.

It is submitted that present claims 1, 4 and 6 are patentably distinct from the claims of copending U.S. Patent Application No. 10/526,065. With regard to claims 1, 4 and 6 of the instant application, all of claims 1, 4 and 6 are directed to a patch, comprising: a backing layer; and an adhesive layer disposed on the backing layer, the adhesive layer comprising a drug and an adhesive base agent comprising a styrene-isoprene-styrene block copolymer, 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the weight ratio of the content of the styrene-isoprene-styrene block copolymer to 2-ethylhexyl acrylate-vinyl acetate copolymer is from 1:1 to 9:1, a basic nitrogen-containing polymer comprising a basic nitrogen and having no adhesion properties at normal temperature, the basic nitrogen-containing polymer being selected from the group consisting of methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate terpolymer, and polyvinyl acetal diethylamino acetate, and an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid, wherein the patch is configured to have a skin permeation rate of from about 1.5

$\mu g/cm^2/hr$ to about 3.2 $\mu g/cm^2/hr$ and to have improved adhesion, cohesion or stability.

Claims 1 and 3-11 of copending U.S. Patent Application No. 10/526,065 do not recite the specific amount ratio between the SIS block copolymer and 2-EHA-VA copolymer and the specific skin permeation rate required by the presently pending claims 1, 4 and 6 in this application. Accordingly, present claims 1, 4 and 6 are ***patentably distinct*** from claims 1 and 3-11 of copending U.S. Patent Application No. 10/526,065. The Examiner is respectfully requested to withdraw this rejection of pending claims 1, 4 and 6.

If the Examiner continues to assert that a *prima facie* case of obviousness-type double patenting has been shown, Applicants respectfully request that the Examiner ***hold*** this rejection in abeyance until such time as the Examiner indicates there is successful resolution of the claim rejections noted above. Applicants, at that time, will either address the rejection or cancel any conflicting claims in copending U.S. Patent Application No. 10/526,065.

CONCLUSION

Applicants submit that the application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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